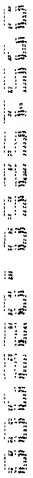
What is claimed is:



Claims

1. A protein comprising a fibronectin type III domain having at least one randomized loop, said protein being characterized by its ability to bind to a compound that is not bound by the corresponding naturally-occurring fibronectin.

2. The protein of claim 1, wherein said fibronectin type III domain is a mammalian fibronectin type III domain.

3. The protein of claim 2, wherein said fibronectin type III domain is a human fibronectin type III domain.

4. The protein of claim 1, wherein said protein comprises the tenth module of said fibronectin type III domain (^{10}Fn3).

5. The protein of claim 4, wherein said compound binding is mediated by one ^{10}Fn3 loop.

6. The protein of claim 4, wherein said compound binding is mediated by two ^{10}Fn3 loops.

7. The protein of claim 4, wherein said compound binding is mediated by three ^{10}Fn3 loops.

8. The protein of claim 4, wherein the second loop of said ^{10}Fn3 is

extended in length relative to the naturally-occurring module.

9. The protein of claim 4, wherein said ^{10}Fn3 lacks an integrin-binding motif.

10. The protein of claim 9, wherein said integrin-binding motif is replaced by an amino acid sequence comprising a basic amino acid-neutral amino acid-acidic amino acid motif.

11. The protein of claim 10, wherein said integrin-binding motif is replaced by an amino acid sequence comprising serine-glycine-glutamate.

12. The protein of claim 1, wherein said protein lacks disulfide bonds.

13. The protein of claim 1, wherein said protein is part of a fusion protein.

14. The protein of claim 13, wherein said fusion protein further comprises an immunoglobulin F_c domain.

15. The protein of claim 13, wherein said fusion protein further comprises a complement protein.

16. The protein of claim 13, wherein said fusion protein further comprises a toxin protein.

17. The protein of claim 13, wherein said fusion protein further comprises an albumin protein.

18. The protein of claim 1, wherein said protein is covalently bound to a nucleic acid.

19. The protein of claim 18, wherein said nucleic acid encodes said protein.

20. The protein of claim 18, wherein said nucleic acid is RNA.

21. The protein of claim 1 or 18, wherein said protein is immobilized on a solid support.

22. The protein of claim 21, wherein said protein is immobilized on said solid support as part of an array.

23. The protein of claim 21, wherein said solid support is a chip or bead.

24. The protein of claim 1, wherein said protein is a multimer.

25. The protein of claim 1 or 9, wherein said protein is formulated in a physiologically-acceptable carrier.

26. A nucleic acid encoding the protein of claim 1 or 4.

27. The nucleic acid of claim 26, wherein said nucleic acid is DNA.

28. The nucleic acid of claim 26, wherein said nucleic acid is RNA.

29. A method for generating a protein comprising a fibronectin type III domain which is pharmaceutically acceptable to a mammal, said method comprising removing an integrin-binding domain from said fibronectin type III domain.

30. The method of claim 29, wherein said integrin binding motif is replaced by an amino acid sequence comprising a basic amino acid-neutral amino acid-acidic amino acid motif.

31. The protein of claim 30, wherein said integrin-binding motif is replaced by an amino acid sequence comprising serine-glycine-glutamate.

32. The method of claim 29, wherein said at least one loop of said fibronectin type III domain is randomized.

33. The method of claim 29, wherein said protein comprises the tenth module of said fibronectin type III domain.

34. The protein of claim 29, wherein said protein is part of a fusion

protein.

35. The protein of claim 34, wherein said fusion protein further comprises an immunoglobulin F_c domain.

36. The protein of claim 34, wherein said fusion protein further comprises a complement protein.

37. The protein of claim 34, wherein said fusion protein further comprises a toxin protein.

38. The protein of claim 34, wherein said fusion protein further comprises an albumin protein.

39. The method of claim 29, wherein said mammal is a human.

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40. A method for obtaining a protein which binds to a compound, said method comprising:

(a) contacting said compound with a candidate protein, said candidate protein comprising a fibronectin type III domain having at least one randomized loop, said contacting being carried out under conditions that allow compound-protein complex formation; and

(b) obtaining, from said complex, said protein which binds to said compound.

41. A method for obtaining a compound which binds to a protein, said protein comprising a fibronectin type III domain having at least one randomized loop, said method comprising:

(a) contacting said protein with a candidate compound, said contacting being carried out under conditions that allow compound-protein complex formation; and

(b) obtaining, from said complex, said compound which binds to said protein.

42. The method of claim 40, said method further comprising randomizing at least one loop of said fibronectin type III domain of said protein obtained in step (b) and repeating said steps (a) and (b) using said further randomized protein.

43. The method of claim 41, said method further comprising modifying said compound obtained in step (b) and repeating said steps (a) and (b) using said further modified compound.

44. The method of claim 40 or 41, wherein said compound is a protein.

45. The method of claim 40 or 41, wherein said fibronectin type III domain is a mammalian fibronectin type III domain.

46. The method of claim 45, wherein said fibronectin type III domain is a human fibronectin type III domain.

47. The method of claim 40 or 41, wherein said protein comprises the tenth module of said fibronectin type III domain (^{10}Fn3).

48. The method of claim 47, wherein said compound binding is mediated by one ^{10}Fn3 loop.

49. The method of claim 47, wherein said compound binding is mediated by two ^{10}Fn3 loops.

50. The method of claim 47, wherein said compound binding is mediated by three ^{10}Fn3 loops.

51. The method of claim 47, wherein the second loop of said ^{10}Fn3 is extended in length relative to the naturally-occurring module.

52. The method of claim 47, wherein said ^{10}Fn3 lacks an integrin-binding motif.

53. The method of claim 40 or 41, wherein said protein is covalently bound to a nucleic acid.

54. The method of claim 53, wherein said nucleic acid encodes said protein.

55. The method of claim 53, wherein said nucleic acid is RNA.

56. The method of claim 40, wherein said compound is immobilized on a solid support.

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57. The method of claim 41, wherein said protein is immobilized on a solid support.

58. The method of claim 56 or 57, wherein said solid support is a column or microchip.

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59. A method for detecting a compound in a sample, said method comprising:

(a) contacting said sample with a protein which binds to said compound and which comprises a fibronectin type III domain having at least one randomized loop, said contacting being carried out under conditions that allow compound-protein complex formation; and

(b) detecting said complex, thereby detecting said compound in said sample.

60. The method of claim 59, wherein said protein is immobilized on a solid support.

61. The method of claim 60, wherein said protein is immobilized on said solid support as part of an array.

62. The method of claim 60, wherein said solid support is a chip or bead.

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63. The method of claim 59, wherein said protein is covalently bound to a nucleic acid.

64. The method of claim 59, wherein said nucleic acid encodes said protein.

65. The method of claim 64, wherein said nucleic acid is RNA.

66. The method of claim 59, wherein said compound is a protein.

67. The method of claim 59, wherein said compound is detected by radiography, fluorescence detection, mass spectroscopy, or surface plasmon resonance.

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